LUD 5253.5-JEL/NDH

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s)	:	Thierry Boon-Falleur et al.
Serial No.	:	08/819,669
Filed	:	March 17, 1997
For	:	TUMOR REJECTION ANTIGEN PRECURSORS, TUMOR REJECTION ANTIGENS AND USES THEREOF
Art Unit	:	1644
Examiner	:	T. Cunningham

#12 Supp 8-8-98

Hon. Commissioner of Patents
and Trademarks
Washington, D.C. 20231

DECLARATION

Sir:

The undersigned, being the inventors of subject matter claims in the above referenced application hereby declare as follows.

1. We submit this declaration in order to correct errors in two of the sequences, i.e., SEQ ID NOS: 7 and 8.

2. Specifically, each of SEQ ID NOS: 7 and 8 present errors in that they are missing a single nucleotide base, a "C", following nucleotides 1377 (SEQ ID NO: 7), and 4633 (SEQ ID NO: 8) (each occurrence).

3. We became aware of these errors in the following way. As is set forth in Examples 20 and 21 of the subject patent application, we isolated a 2.4 kilobase, genomic DNA clone which encodes the molecule referred to as MAGE-1 and then we used this 2.4 kilobase, genomic DNA clone in Northern Blood experiments. We were able to detect a positive band in this way, which was about 1.8 kilobases long. This is reported as Example 21.

4. We also screened cDNA libraries. Our earliest screening experiments did not identify a full length cDNA molecule. Rather, the longest molecule we identified was one that was 1.3 kilobases long. We knew that this molecule would be too short, but it was the longest one we identified, so we proceeded to sequence it. We sequenced along both the sense and antisense strands, to obtain a deduced sequence. Neither the sense nor the antisense strand was sequenced completely. We obtained the sequence corresponding to the region discussed herein from the sense sequence, and secured the correct sequence, i.e., the sequence forth in our amendment. Since the sequence was clearly not complete, we did not include it in our patent application.

5. We also did sequencing work on the 2.4 kilobase genomic clone, discussed above. Again, we sequenced both the sense and antisense strands, but not the complete strand of either,

although the overlap of the strands permitted us to give a complete sequence. The sequence of the region discussed herein was obtained from the antisense sequence and resulted in an error, i.e., the error we seek to correct herein. This work was done on June 4, 1991.

6. Since the 1.3 kb cDNA reported above was clearly incomplete, we carried out further experiments on this cDNA library, using the 1.3 kb cDNA molecule discussed herein as a probe. We identified a 1.7 kb cDNA molecule in this way, which is clearly longer than 1.3 kilobases. Again, we sequenced the molecule, on both sense and antisense strands, using the same overlapping procedure to deduce a complete sequence. The sequence corresponding to the region discussed herein was obtained from the antisense sequence. Again, there was an error - the same one which was presented in the sequence of the gDNA molecule. The cDNA sequencing described herein was carried out on July 4, 1991.

7. Given that we had two clones (the 1.7kb cDNA, and the 2.4 kb gDNA), which agreed with each other, we used this sequence information in the patent application.

8. As part of our ongoing research, we prepared a second cDNA library, using the same source of mRNA which we used to isolate the 1.7 kilobase clone we discussed, supra. We found a cDNA clone which was 10 base pairs longer than the 1.7 kilobase fragment.

9. We were involved in a collaboration with other scientists sometime later, and we sent this 1.7 kilobase plus 10 base pairs clone to our colleagues. Our colleagues sequenced the

cDNA we sent them (i.e., the 1.7 kilobase plus 10 base pairs), after they had transferred it from the vector in which we had sent it to another vector. We also had sent them our incorrect sequence information. When they sequenced the cDNA, they found a one base pair difference. Assuming that the perceived error had been caused by their manipulations, they then sequenced the cDNA we had sent them before transfer to another vector, but found that it was the same as they originally had. In other words, there had been no error caused by their manipulations. They reported their findings to us. This all took place in June, 1993.

10. Within forty eight hours of receiving this information from our colleagues, we sequenced, on both strands, the portion of our 10+1.7 kilobase clone which would have contained the error, and found that the sense sequence agreed with our colleagues. Since the additional 10 bases (as compared to the original 1.7 kilobase clone) were at the 5' end, we knew that the change was not a result of the new 10 bases. When we obtained the antisense sequence of the relevant portion, we found the same problem we had before, i.e., the same base was missing. We now attribute this to a well known phenomenon, which is band compression. This occurs in nucleic acid molecules which are rich in G&C regions. Many references show this. We will provide them on request.

11. We did consider the possibility that an extra nucleotide had been introduced into the 10 base +1.7 kilobase cDNA clone when it was prepared from the mRNA. We were able to eliminate this possibility by sequencing the 1.3 kilobase cDNA molecule referred to supra. This smaller molecule contained the relevant portion of both the 1.7 and 10+1.7 kilobase cDNA

molecules. When we compared the sequences we deduced from the three molecules, the relevant portions of the 1.3 and 10+1.7 kilobase cDNA molecules were identical to each other, while the 1.7 kilobase cDNA molecule lacked the "C" base, as indicated above.

12. When we sequenced the 1.7 kilobase cDNA molecule for the patent application, we did not sequence the portion of the sense strand corresponding to the antisense strand which was later found to have been presented incorrectly. In retrospect, we should have done this, but this realization comes from the benefit of hindsight.

13. We corrected the sequence in the Genbank data bases late in 1993. We simply did not consider any patent matters in terms of corrections. This omission is regretted.

14. The errors arose without any deceptive intent on our part.

15. We hereby declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

LUD 5253.5-JEL/NDH

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LUD 5253.5-JEL/NDH

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LUD 5253.5-JEL/NDE

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